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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/566,292
Filing Date: January 27, 2006
Appellant(s): ALMIRANTE ET AL.

Richard J. Berman
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed July 9, 2010 appealing from the Office action mailed November 23, 2009.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

McIntyre et al. "Losartan, an Orally Active Angiotensis (AT1) Receptor Antagonist: A Review of Its Efficacy and Safety in Essential Hypertension" Pharmacol. Ther. 1997, Vol 74, No 2, Pages 181-194

WO 00/61537	DEL SOLDATO	10-2000
WO 95/09831	DEL SOLDATO	04-1995

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 5-15, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over McIntyre et al. (*Pharmacol. Ther., 1997,* 181-194) in view of Del Soldato (WO 00/61537, referred to below as Del Soldato I) and Del Soldato (WO 95/09831, referred to below as Del Soldato II).

The instant claims are drawn to nitrooxy derivatives of Angiotensin II receptor blocker drugs. The species searched is a derivative of the drug losartan.

McIntyre et al. teach the drug losartan. See the whole document, specifically page 182 for the structure of losartan.

McIntyre et al. do not teach attaching a nitrooxy tether to the drug as instantly claimed.

Del Soldato I teaches that the addition of a nitrooxy tether to drugs such as losartan remove side effects to patients affected by oxidative stress and/or endothelial dysfunctions or to the elderly in general. See pages 6-13. The exact tether that is used

in the elected species is shown in Example 10 on page 84, albeit attached to a bridging component.

Del Soldato II teaches that a nitrooxy tether can be attached directly to a drug such as naproxen. See page 14, line 20 through page 16, line 17.

Therefore, on of ordinary skill in the art would be motivated to take losartan, which is discussed at length by McIntyre et al. and attach the nitrooxy tether as shown by Del Soldato I described as capable of function with losartan, and directly to the drug as taught in Del Soldato II, with a reasonable expectation of success. The motivation for making the change is that he addition of a nitrooxy tether to drugs such as losartan remove side effects to patients affected by oxidative stress and/or endothelial dysfunctions, or to the elderly in general.

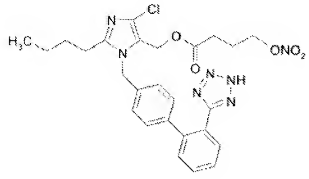
Thus, the claims are *prima facie* obvious over the prior art.

(10) Response to Argument

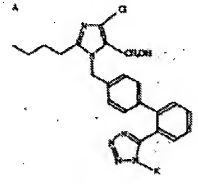
The Appellant has argued that the rejection is improper at least because a *prima facie* case has not been established.

An election of species was made in the application and the Appellant elected without traverse the species 2-butyl-4-chloro-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1H-imidazole-5-methanol 4-nitroxybutanoic acid ester. As a rejection was made on the elected species, the provisional election was given effect and the search was limited to the elected species. The species is the drug known by the generic name losartan with a 4-nitrooxybutyl ester tail attached to the 5-methanol substitution on the

imidazole ring and is represented by the structure



The Appellant is correct that McIntyre et al. only teach losartan without the



nitrooxy tether, which is represented by the structure . See page 182 of McIntyre et al.

Losartan is one of many drugs envisioned by Del Soldato I as capable of improvement by addition of a nitrooxy tether. Specifically, Del Soldato I teaches that the addition of a nitrooxy tether to drugs such as losartan remove side effects to patients affected by oxidative stress and/or endothelial dysfunctions or to the elderly in general. See pages 6-13. This allows drugs to be administered in higher doses to patients who normally have side effects to drugs which leads to more effective treatments of various medical conditions.

Del Soldato I, as stated by the Appellant, teaches three tests for the evaluation of drugs to be modified according to the invention. However, the Appellant has mischaracterized the results of the tests with omeprazol or misoprostol. The Appellant has stated on page 6 of the brief that these drugs do not satisfy any of the tests, but Del Soldato I only teaches results with omeprazole for Test 3, the L-NAME test. No results are described with omeprazole with the other two tests. See pages 34-35. As a drug only has to meet one of the 3 tests of Del Soldato I to be qualified as to be worthy of modification by the addition of a nitrooxy tether, omeprazole is still a possibility since results from the other two tests are not known from the disclosure of Del Soldato I. Additionally, a drug can fail one test and yet pass another of the tests. Mesalamine does not qualify under Test 2, the CIP test, however qualifies under Test 1, the NEM test. See pages 34-35. Therefore, a negative result on one test cannot disqualify a drug from modification by Del Soldato I. A drug must have a negative result on all three tests.

Del Soldato I provides a list of drugs that are capable of modification. As acknowledged by the Appellant, this list includes losartan. See pages 6 and 41. Del Soldato I provides a finite number of identifiable, predictable solutions to the problem of improving drugs which can produce side effects to patients sensitive to oxidative stress, especially the elderly. The drug is attached to the tether either through a carboxylic acid group, or though an XH group where X is O, S, or NR1c as defined on page 7 of Del Soldato I. As is shown by the structure in McIntyre et al., there is only one place in losartan that can be modified by this rationale, namely the methanol group in the 5-

position of the imidazole ring. While Del Soldato I does not show any test results with losartan in the disclosure, Del Soldato I does not disqualify any drugs from modification since no drugs are shown to have failed all three of the prescribed tests. Additionally, the exact tether that is used in the elected species is shown in Example 10 on page 84 of Del Soldato I, albeit attached to a bridging component.

The companion teachings of Del Soldato II teach that this nitrooxy tether can be attached directly to a drug such as naproxen. See page 14, line 20 through page 16, line 17. Therefore, the need for a bridging group as described in Del Soldato I is eliminated.

Hence, the Examiner believes that the *prima facie* case of obviousness in intact because Del Soldato I provides a finite list of drugs that are able to be modified to meet a defined design need, that losartan is the only drug mentioned under "anti-angiotensin drugs" on page 6 of Del Soldato I, that Del Soldato I teach the exact same nitrooxy tether as used in the elected species on page 84, that losartan is a well known drug as taught by McIntyre et al., and that Del Soldato II teaches that this nitrooxy tether can be attached directly to a drug to meet the same design needs. The Examiner believes that the conclusion of obviousness has been made properly with respect to the Graham vs. John Deere factors.

The Appellant has not shown any evidence of secondary considerations. The Examiner believes that a *prima facie* case of obviousness has been made. In the absence of any evidence of secondary considerations, the Examiner maintains that the claims are *prima facie* obvious over the prior art.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Joseph R Kosack/

Primary Examiner, Art Unit 1626

Conferees:

/Joseph K. McKane/

Supervisory Patent Examiner, Art Unit 1626

/James O. Wilson/

Supervisory Patent examiner